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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,421	01/22/2001	Michael J. Shamblott	JHU1750-1	9551

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/767,421	SHAMBLOTT ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,13,15,16,22,23,25-29,32 and 35-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,13,15,16,22,23,25-29,32 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *January 22, 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed April 25, 2008 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1, 10, 13, 15, 16, 22, 23, 25-29, 32, 35-38 are pending.

The term "EBD-derived cell" means an undifferentiated cell that composes an embryoid body.

The Examiner, in attempting to be clear, highlighted citings in the art in bold typeface for the new claim limitations.

The rejection of claims 1, 9-13, 15, 16, 22-32 and 34-38 under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement made in the office action mailed January 28, 2008 is withdrawn in view of applicant's amendments.

The rejection of claims 1, 9-13, 15, 16, 22-32 and 34-38 under 35 U.S.C. 112, second paragraph made in the office action mailed January 28, 2008 is withdrawn in view of applicant's amendments.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10, 13, 15, 16, 22, 23, 25-29, 32 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22 states "reduced-serum media." However, the specification fails to provide a definition of the term such that the artisan could realize the metes and bounds of the claim.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10, 13, 15, 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,453,357 issued September 26, 1995 (Hogan) in view of Shamblott et al (1998) Proced. Natl. Acad. Sci. 95, pp. 13726-13731 (ref. AE) for reasons set forth in the office action mailed January 28, 2008.

Hogan teaches mouse embryoid body cells isolated from mouse embryoid bodies (EB's), rounded colonies of densely packed ES-like cells, produced by the culture of mouse primordial germ cells (col. 6, lines 19-49). Hogan describes the picking of single clones of EB-derived mouse cells, indicating clonal selection from a single EB-derived cell (col. 8, lines 5-9). **Further Hogan teaches culturing PGC's in media containing (col. 6, lines 36-40). Hogan teaches PGC culture media contains 15% FBS (col. 6, lines 29-33). As the specification provides no clear definition of reduced serum, this teaching of Hogan is reduced. The specification provides neither a range of media concentrations that define "reduced serum" nor does the specification provide a comparison concentration.** Hogan offers motivation in stating ES cells from other mammals, such as humans, can be produced using the

methods described therein for mouse (col. 5, lines 3-5 and col. 9, lines 18-11). Hogan offers additional motivation in stating derivatives of human ES cells, produced by the method disclosed therein, could treat neurodegenerative disease (col. 5, lines 32-34). Hogan also teaches the mouse EBD-cells to undergo at least 20 population doublings (col. 8, lines 14-16). Hogan further teaches that LIF make not be required for the maintenance of ES cells, which are interpreted to be the cells of the claims (col. 4, lines 55-67).

Shamblott teaches embryoid bodies (EB's) produced from human primordial germ cells (hPGC's) (13729, col. 1, parag. 1-12). Shamblott offers motivation in stating the human pluripotent stem cells produced therein would provide for studies of human embryogenesis, transplantation therapies, and defining culture conditions and differential gene expression for cell-type differentiation (page 13730, col. 1, parag. 2, lines 1-8).

As the presently claimed cells are derived from human primordial germ cells, the ordinary artisan at the time of filing would have reasonably expected the physiological characteristics to be the same for the claimed cells and those of Hogan even given species differences. Thus, the cells of Hogan in view of Shamblott undergo at least 30 or at least 60 population doublings, proliferate under conditions nonpermissive for the proliferation of human EG cells, proliferate under culture conditions lacking LIF, a fibroblast feeder layer, or both, and transfectable with a retrovirus, lentivirus or both. There is no evidence to the contrary on the record. Products obvious over those in the art would be expected to have the same properties absent evidence to the contrary.

Therefore at the time of the present invention, it would have been obvious to produce human EBD-cells in view of the production of mouse EBD-cells as taught by Hogan in view of Shamblott teachings human EB's. The prior art offers the requisite teachings, suggestions and motivation to combine, and a reasonable expectation of success.

Applicant argues the claims recited a human EBC cell characterized by forming disaggregated single cells upon dissociation from EB's and adhering to defined extracellular matrix components lacking a feeder layer and lacking LIF and having the ability to be maintained in culture on the defined extracellular matrix components in the absence of a feeder layer for at least 30 population doublings with being immortal. Applicant argues the cited art does not teach these limitations. Applicant argues Hogan indicates that a feeder cell and LIF were always used to culture the PCG cells, as does Shamblott. Applicant argues the claimed cell and those of the cited art would not be expected to have the same physiological characteristics. Applicant argues the maximum population doubling times varies between species, which is due to progressive telomere shortening. Applicant argues the mouse PGC's in Hogan were grown on feeder layers for no more than 20 doublings. Applicant argues mouse EBD cannot double for thirty population doublings. These arguments are not persuasive.

The ability to grow in the absence of LIF or without feeder cells is not a characteristic of the cells per se, but on culture conditions. Further, applicant has not provided any evidence the EBD cells produced by combining Hogan and Shamblott would require LIF or feeder cells. All applicant argues is the combined art never

attempted to grow the EBD's without LIF or without feeder cells. Newly recognized properties of a product do not give patentability to the old product. The characteristics argued by applicant are all related to culture conditions, and not any structure associated with the cells. While all cells have a population doubling limit, applicant has not provided any evidence that the claimed cells and those of the combination of art have a structural difference. The cells claimed and those of the combination of art came from the same tissue source, human PGC's, by indistinguishable methods. Thus, the cells are the same. In a side by side comparison, no difference between the cells is evident. Any differences in population doubling could also be attributed to culture conditions. The motivation to combine is for the production of human EBD cells. Since a product and its properties cannot be separated, products of similar origin and production, as is the case here, are reasonably expected to be the same product. Thus, human EBD cells produced by the combination of Hogan and Shamblott would have the characteristics argued. Applicant has provided no evidence that cells produced by a combination of Hogan and Shamblott do not have the same characteristics, such as the same population doublings when grown under the same conditions. If applicant has any such evidence it should be presented in an affidavit.

Claims 22, 25-29, 32, 35, 27 and 30-32, 35, 36 and 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,453,357 issued September 26, 1995 (Hogan) in view of Shamblott et al (1998) Proced. Natl. Acad. Sci. 95, pp. 13726-13731 (ref. AE) for reasons set forth in the office action mailed January 28, 2008.

Hogan teaches a method of producing EBD-cells comprising culturing primordial

germ cells to form an embryoid body), rounded colonies of densely packed ES-like cells, digesting the embryoid body with trypsin to provide EBD-cells and culturing the EBD-cells in media comprising hFGF2 (col. 6, lines 20-48). Hogan describes the picking of single clones of EB-derived mouse cells, indicating clonal selection from a single EB-derived cell (col. 8, lines 5-9). Hogan also teaches the mouse EBD-cells to undergo at least 20 population doublings, which encompasses 30 population doublings (col. 8, lines 14-16). Hogan further teaches that LIF make not be required for the maintenance of ES cells, which are interpreted to be the cells of the claims (col. 4, lines 55-67). LIF is required for the growth of EG cells as stated in the specification (specification, page 8m lines 2-3). **Further Hogan teaches culturing PGC's in media containing (col. 6, lines 36-40). Hogan teaches PGC culture media contains 15% FBS (col. 6, lines 29-33). As the specification provides no clear definition of reduced serum, this teaching of Hogan is reduced. The specification provides neither a range of media concentrations that define "reduced serum" nor does the specification provide a comparison concentration.** Hogan teaches culture of EBD-cells on feeder cells, which is a matrix. Hogan offers motivation in stating ES cells from other mammals, such as humans, can be produced using the methods described therein for mouse (col. 5, lines 3-5 and col. 9, lines 18-11). Hogan offers additional motivation in stating derivatives of human ES cells, produced by the method disclosed therein, could treat neurodegenerative disease (col. 5, lines 32-34).

Shamblott teaches embryoid bodies (EB's) produced from human primordial germ cells (hPGC's) (13729, col. 1, parag. 1-12). Shamblott offers motivation in stating

the human pluripotent stem cells produced therein would provide for studies of human embryogenesis, transplantation therapies, and defining culture conditions and differential gene expression for cell-type differentiation (page 13730, col. 1, parag. 2, lines 1-8).

Thus, at the time of filing, it would have been obvious to the ordinary artisan to follow the method of Hogan to produce human EBD cells given the method of producing human EB's from hPGC culture as taught by Shamblott given the teachings and motivations provided. The cited prior art provides the requisite teaching, suggestion and motivation, as well as a reasonable expectation of success.

Applicant argues the combination of Hogan and Shamblott would lead only to a method where human EBD cells were cultured on feeder cells and in the presence of LIF. This argument is not persuasive.

The claims, as written, have no recitation of without LIF and/or in the absence of feeder cells. Reference to the absence of feeder cells is part of a wherein clause described the characteristics of EBD cells. Applicant ought to consider amending the claims to insert active method steps that distinguish the method claims from those of the prior art. This may overcome the art rejection over the method claims.

Claims 22, 27-29, 36 and 37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,453,357 issued September 26, 1995 (Hogan) in view of Shamblott et al (1998) Proced. Natl. Acad. Sci. 95, pp. 13726-13731 (ref. AE) further in view of Rohwedel et al (1996) Cell Biol. Internat. 20, pp. 579-587 (ref. AC) for reasons set forth in the office action mailed January 28, 2008.

Hogan teaches a method of producing EBD-cells comprising culturing primordial germ cells to form an embryoid body), rounded colonies of densely packed ES-like cells, digesting the embryoid body with trypsin to provide EBD-cells and culturing the EBD-cells in media comprising h bfgf2 (col. 6, lines 20-48). **Further Hogan teaches culturing PGC's in media containing (col. 6, lines 36-40). Hogan teaches PGC culture media contains 15% FBS (col. 6, lines 29-33). As the specification provides no clear definition of reduced serum, this teaching of Hogan is reduced. The specification provides neither a range of media concentrations that define "reduced serum" nor does the specification provide a comparison concentration.** Hogan offers motivation in stating ES cells from other mammals, such as humans, can be produced using the methods described therein for mouse (col. 5, lines 3-5 and col. 9, lines 18-11). Hogan offers additional motivation in stating derivatives of human ES cells, produced by the method disclosed therein, could treat neurodegenerative disease (col. 5, lines 32-34).

Shamblott teaches embryoid bodies (EB's) produced from human primordial germ cells (hPGC's) (13729, col. 1, parag. 1-12). Shamblott offers motivation in stating the human pluripotent stem cells produced therein would provide for studies of human embryogenesis, transplantation therapies, and defining culture conditions and differential gene expression for cell-type differentiation (page 13730, col. 1, parag. 2, lines 1-8).

Rohwedel teaches the culture and expansion of mouse EB cells on tissue culture plates coated with gelatin for morphological studies (page 580, col. 2, parag. 1, lines 14-

18). Morphological studies are a part of a study of embryogenesis. It is noted that gelatin is a hydroxylation product of collagen I.

Thus, at the time of filing, it would have been obvious to the ordinary artisan to follow the method of Hogan to produce human EBD cells given the method of producing human EB's from hPGC culture as taught by Shamblott, culturing the EBD cells on collagen I coated plates given the teachings and motivations provided. The cited prior art provides the requisite teaching, suggestion and motivation, as well as a reasonable expectation of success.

Applicant argues Rohwedel grew cells on plates coated with gelatin to differentiate them into somatic cells. Applicant argues Rohwedel does not teach maintaining EBD cells in culture on a defined substrate. This argument is not persuasive.

The claims do not require an length of time for the EBD cells to be maintained. As Rohwedel had to have maintained the cells for some period time prior to the onset of somatic cell differentation, Rohwedel meets the limitation of the claim.

Claims 25 and 26 are free of the prior art. At the time of filing the prior art did not teach or suggest methods of obtaining a human EBD cell comprising culturing resulting EBD cells in the particular media claimed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

August 6, 2008